



## CORRESPONDENCE

### Oncological aspects related to non-surgical treatment of basal cell carcinoma. Comments on: chemotherapeutical treatment of basal cell carcinoma with bleomycin via microinfusion of the drug into the skin (MMP®)☆



Dear Editor,

As the incidence of basal cell carcinoma (BCC) is increasing, investigations into treatments that are less costly and complex than surgery are invaluable.<sup>1</sup> Therefore, we read with interest the article by Pacola et al., who performed the administration of intratumoral bleomycin, using a tattoo machine, in a series of 98 lesions followed for six months, resulting in a histopathological cure rate of 96.9% (95% CI 92.9%–99.0%). And we would like to comment on certain oncological aspects regarding the generalization of the results.<sup>2</sup>

Intratumoral bleomycin, in association with electrochemotherapy, and/or intravenous bleomycin were reported to be effective in the treatment of BCC in 32 previous studies, achieving cure rates of 92% after two months of follow-up, with recurrences not precluding retreatment.<sup>3</sup> This may be invaluable in patients without clinical conditions for surgery; however, the lack of randomized controlled trials comparing it with excisional surgery does not allow critical insight into the cost-effectiveness of chemotherapy infusion in the treatment of common BCC.

Due to the low mitotic rate, the assessment of histopathological recurrence is an adequate outcome for investigating the efficacy of therapies in BCC. However, the recurrence rate increases with the years of follow-up, and only 32% of them are detected in the first year following surgery,<sup>4</sup> which makes the evaluation at six months insufficient for a satisfactory comparison with the oncological literature. Recurrence may be clinically imperceptible for many months, meaning that punch biopsy sampling, as used by Pacola et al., may underestimate its occurrence in another topography of the lesion. Especially because the scarring aspect promoted by bleomycin can make clinical and/or dermoscopic evaluation of recurrence difficult.

Ideally, a follow-up of more than three years and histopathological sampling of the entire scar area is necessary for a correct estimate of the cure rate.

Additionally, factors associated with BCC recurrence are very diverse, including size, topography, margin size, histopathological type, and immunosuppression. The authors included high-risk lesions in the case series, applied different safety margin sizes, and treated lesions greater than 3 mm in depth, which are beyond the reaching scope of the tattoo machine needles. Furthermore, BCC lesion sampling by biopsy does not allow an accurate estimation of the depth and infiltrative components of the BCC as a whole.<sup>5</sup>

Finally, it is worth mentioning the high rate (19%) of loss to follow-up of patients included in the case series, without clarification whether it was due to treatment, adverse effects, or recurrence of lesions.

### Financial support

None declared.

### Authors' contributions

Ivanka Miranda de Castro Martins: Design of the study, drafting and editing of the manuscript and approval of the final version of the manuscript.

Ana Cláudia Cavalcante Espósito: Design of the study, drafting and editing of the manuscript and approval of the final version of the manuscript.

Hélio Amante Miot: Design of the study, drafting and editing of the manuscript and approval of the final version of the manuscript.

### Conflicts of interest

None declared.

### References

- Schmitt JV, Chinem VP, Marques ME, Miot HA. Increase in the incidence of basal cell carcinoma in a university hospital between 1999 and 2009. *An Bras Dermatol.* 2011;86:375–7.
- Pacola PR, Rostey RRL, Rizzo FFA. Chemotherapeutical treatment of basal cell carcinoma with bleomycin via microinfusion of the drug into the skin (MMP®). *An Bras Dermatol.* 2023;98:587–94.

☆ Study conducted at the Faculty of Medicine, Universidade Estadual Paulista, Botucatu, SP, Brazil.

- Hendel K, Jemec GBE, Haedersdal M, Wiegell SR. Electrochemotherapy with bleomycin for basal cell carcinomas: a systematic review. *J Eur Acad Dermatol Venereol.* 2021;35:2208–15.
- Ocanha JP, Dias JT, Miot HA, Stolf HO, Marques ME, Abbade LP. Relapses and recurrences of basal cell face carcinomas. *An Bras Dermatol.* 2011;86:386–8.
- Cerci FB, Kubo EM, Werner B. Comparison of basal cell carcinoma subtypes observed in preoperative biopsy and Mohs micrographic surgery. *An Bras Dermatol.* 2020;95:594–601.

Ivanka Miranda de Castro Martins <sup>a</sup>,  
Ana Cláudia Cavalcante Espósito <sup>b</sup>,  
Hélio Amante Miot <sup>a,\*</sup>

<sup>a</sup> Department of Infectology, Dermatology, Imaging Diagnosis and Radiotherapy, Faculty of Medicine, Universidade Estadual Paulista, Botucatu, SP, Brazil

<sup>b</sup> Service of Dermatology, Universidade do Oeste Paulista, Presidente Prudente, SP, Brazil

\* Corresponding author.

E-mail: helio.a.miot@unesp.br (H.A. Miot).

Received 13 August 2023

Available online 8 December 2023

<https://doi.org/10.1016/j.abd.2023.08.007>

0365-0596/ © 2023 Sociedade Brasileira de Dermatologia.

Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## Oncological aspects related to the non-surgical treatment of basal cell carcinoma – Response<sup>☆</sup>

Dear Editor,

The authors are grateful for the comments regarding the article: Chemotherapeutic treatment of basal cell carcinoma with bleomycin via microinfusion of the drug into the skin (MMP®)<sup>1</sup> and are aware of the main limitation of the study, which was the six-month follow-up. These controls were carried out after six months, through spindle biopsies and histopathology, which is the standard method for diagnosis.<sup>2</sup> It is also known that only micrographic surgery using the Munich technique could assertively confirm the absence of disease throughout the scar, even five years after the treatment.<sup>3</sup>

Although the study ended in 2021, the patients continue to be monitored, so that after five years this cure rate can be updated and a new report can be published.

Regarding safety margins, it is our knowledge that low-risk lesions require at least 4 mm and high-risk lesions require at least 6–7 mm,<sup>4,5</sup> and these guidelines were followed for the treated lesions.

Regarding tumor thickness, as mentioned before, few lesions with tumor thickness >3 mm were included. In fact, only one of them showed recurrence within six months. In this case, this decision was made because it was located in a low-risk area and was elevated above skin level. This observation is necessary to recall that it was a criterion of the study to perform a shave biopsy in all lesions that were elevated above the normal skin surface (safety margin region) so that the penetrating needle reached the same depth both in the lesion and in the safety margin. And once the lesion is “leveled”, the tumor thickness decreases.

Considering the low risk of metastasis of basal cell carcinoma and the greater risk of local recurrence, it was decided to include such lesions, as well as lesions in high-risk areas so



that there was a broader view of the therapeutic potential of the bleomycin technique in this study.

The high rate (19%) of patients lost to follow-up was due to factors beyond the authors knowledge. And, in principle, not associated with any type of complication, so it cannot be stated or concluded that it had any relationship with the initial treatment and may be the result of sociocultural characteristics of the attended population. Therefore, these data were excluded from the analyses. It is important to emphasize that all patients were advised to return for follow-up. And, according to the commitment established through the FIC form, the post-surgical follow-up during five years was our responsibility, as well as offering other treatment options in case of recurrence.

We are thankful for the considerations, as they are always important and relevant for our improvement.

### Financial support

None declared.

### Authors' contributions

Paulo Rodrigo Pacola: Approval of the final version of the manuscript; design and planning of the study; drafting and editing of the manuscript.

### Conflicts of interest

None declared.

### References

- Pacola PR, Rostey RRL, Rizzo FFA. Chemotherapeutic treatment of basal cell carcinoma with bleomycin via microinfusion of the drug into the skin (MMP®). *An Bras Dermatol.* 2023;98:587–94.
- Teixeira AKS, Vasconcelos JLA. Histopathological profile of patients diagnosed with malignant tumors assisted in a hospital of reference of agreste pernambucano. *J Bras Patol Med Lab.* 2019;55:87–91.
- Lacerda PN, Lange EP, Luna NM, Miot HA, Nogueira VSN, Abbade LPF. Recurrence rate of basal cell carcinoma among different

<sup>☆</sup> Study conducted at the Department of Dermatology, Hospital Universitário Júlio Muller, Cuiabá, MT, Brazil.